UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/284,555	05/26/1999	SUSAN CROLL-KALISH	REG471-PCT-U	2473

7590 04/21/2005

Linda O. Palladino
REGENERON PHARMACEUTICALS INC
777 OLD SAW MILL RIVER ROAD
TARRYTOWN, NY 10591

EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/284,555	CROLL-KALISH ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgment of the amendment, filed 4-30-02 is made. The amendment amended claims 1, 6, 12 and 18. Therefore, claims 1-18 are pending. As a note, Applicants in the "Marked-up Version" of the claims showed the existence of claims 19-21. This is incorrect since these claims were in Amendment filed 5-26-1999.

Claim Rejections - 35 USC § 101

2. Claims 1-6 remain rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966) for the reasons set forth in the previous office action and the reasons set forth below.

Applicants stated that the claims had been amended so as to overcome the rejection.

Its seems that the Applicants misconstrued the rejection. The rejection was made with regards to the "Use of" terminology. The MPEP states "[i]n view of the split of authority as discussed above, the most appropriate course of action would be to reject a "use" claim under alternative grounds based on 35 U.S.C. 101 and 112." Applicants are requested to review section 2173.05(q) for further information. Applicants should amend the claims to a known statutory class of invention such as "product," "processs" or "method."

3. As stated in the previous office acton, a use, perse is not statutory claim of invention. These claims have been read as if in proper process of use format (applicant is required to properly amend the claims) as the following grounds of rejection under 35 USC 112, 102 and 103.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-6 and 13-17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in the previous office action and the reasons set forth below.

Note that the rejection of claim 12 has been withdrawn.

Applicants argue that the claims have been amended to so as to not to recite enhancement and thereby obviating the rejection. Moreover, claims 1-6 have been amended to recite steps involved thereby obviating the rejection.

Applicants arguments filed have been considered but have not been found persuasive.

The claims 13-17 still read "[a] method for enhancing the intracerebral, extracerebral, intraparenchymal, intracerebraventricular, or intrathecal delivery." It is still the reference point to measure the enhancement. The claims do not recite a point of reference that accurately determines the enhancement of the intracerebral, extra cerebral, intrapareenchymal, intracerebraventricular or intrathecal delivery of the growth factor.

Claims 1-6 provide for the use of a soluble form of a receptor. Its seems that the Applicants misconstrued the rejection. The rejection was made with regards to the "Use of"

terminology. The MPEP states "[i]n view of the split of authority as discussed above, the most appropriate course of action would be to reject a "use" claim under alternative grounds based on 35 U.S.C. 101 and 112."

The rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 7-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Zheng et al. for the reasons set forth in the previous office action and the reasons set forth below.

6.

The claims are drawn to compositions comprising growth factor(s) and a soluble form of a receptor for said growth factor(s).

Applicants argue that the reference does not anticipate the claimed invention teaches away from the applications invention because the coadministratoin of the neurotrophins with TrkB-IgG and TrkC-IgG resulted in inhibition of the survival promoting effects of NT-4/5. The claimed invention is drawn to growth factors that enhance rather than inhibit by the presence of the soluble form of the receptor.

Applicants arguments have been considered but have not been found persuasive.

The rejected claims are drawn to "[a] pharmaceutitcal composition comprising a growth factor; soluble form of a receptor for said growth factor; and a pharmaceutically acceptable vehicle."

(see claim 1). As Applicants have acknowledged, the reference the reference "teaches the administration of neutrophins, including NGF, BDNF, NT3 and NT-4/5 with TrkB-IgG." Thus, the reference meets the limitation of the claims. In fact, where "[l]anguage that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation." These include statements of intended use or field of use. Here the instant claims are drawn to only a pharmaceutical formulation and since the reference teaches that specific formulation, the reference anticipates the claimed invention.

Rejection is maintained.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3, 7-9 and 13-~~16~~18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prisell et al. in view of Sable et al. for the reasons set forth in the previous office action and the reasons set forth below.

The claims are drawn to methods of use of and composition(s) comprising a growth factors and a soluble form of a receptor for said growth factors.

Applicants argue that the composition contains materials such as hyaluronic acid as a cross-liked matrix with the receptor. "Such composition would not be brain-compatible and thus there could be no omotivation to combine with the delivery system of Sable for the treatment of neural disorders." Thus, the rejection cannot stand.

Applicants arguments have been considered but have not been found persuasive.

If a prima facie case is established, the burden shifts to applicant to come forward with rebuttal evidence or argument to overcome the prima facie case. See, e.g., Bell, 991 F.2d at 783-84, 26 USPQ2d at 1531; Rijckaert, 9 F.3d at 1532, 28 USPQ2d at 1956; Oetiker, 977 F.2d at 1445, 24 USPQ2d at 1444. Short of opinions, Applicants have not furnished any evidence to conclude that hyluronic acid is not brain compatible. To the contrary, it is conventionally known in the art to use hyluronic acid as a pharmaceutical excipient for delivery of therapeutics to the brain. For example Falk et al. disclose, Administration of dimethyl sulfoxide (DMSO) in amounts of less than 100 gm daily in a 10% solution in hyaluronic acid (sodium hyaluronate) -300-500 mg to reduce acute brain and spinal edema (see col. 17, lines 13-17). Furthermore, the reference of Hockfield et al. teach that Hyaluronan (also called hyaluronic acid or hyaluronate) is a negatively charged high-molecular-weight linear polysaccharide built from repeating disaccharide units (Laurent, T. C., and Fraser, J. R. E., FASEB (Fed. Am. Soc. Expo Biol.) 6:2397-2404 (1992)). Hyaluronan is ubiquitously distributed in the extracellular matrices of all tissues, including brain, and is believed to have several

functions, including the organization of water and extracellular proteins (ibid.) (See col. 1, lines 33-45). Given that hyaluronic acid is found in the extracellular matrix of the brain, it would be reasonable to conclude that it is brain compatible. Accordingly, the references render obvious the claimed invention.

As a note, both reference of Hockfield and Falk et al. have been cited only to rebut Applicants contention that Hyaluronic acid is not brain compatible. These references have not been incorporated into the call of the rejection. The rejection is still Claims 1-3, 7-9 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prisell et al. in view of Sable et al.

The rejection is maintained.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can normally be reached on (571) 272-0974. The fax phone number of this group is (571)-273-8300.

4/4/05

Anish Gupta
Patent Examiner